

Translation

PATENT COOPERATION TREATY

PCT/JP2003/008420



PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference ONF-4610PCT	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/JP2003/008420	International filing date (day/month/year) 02 July 2003 (02.07.2003)	Priority date (day/month/year) 03 July 2002 (03.07.2002)
International Patent Classification (IPC) or national classification and IPC A61K 45/00, 38/17, 39/395, 31/7088, A61P 31/00, 35/00, 35/04, 37/04, C12N 5/10, C12Q 1/02, G01N 33/50, A01K 67/027		
Applicant ONO PHARMACEUTICAL CO., LTD.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising: a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows: <div style="margin-left: 40px;"><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</div> b. <input type="checkbox"/> (sent to the International Bureau only) a total of _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items: <div style="margin-left: 20px;"><input checked="" type="checkbox"/> Box No. I Basis of the report <input type="checkbox"/> Box No. II Priority <input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <input type="checkbox"/> Box No. IV Lack of unity of invention <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement <input checked="" type="checkbox"/> Box No. VI Certain documents cited <input type="checkbox"/> Box No. VII Certain defects in the international application <input type="checkbox"/> Box No. VIII Certain observations on the international application</div>

Date of submission of the demand 06 January 2004 (06.01.2004)	Date of completion of this report 16 September 2004 (16.09.2004)
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

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Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

- ☒ The international application as originally filed/furnished
- ☐ the description:
- pages _____, as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ the claims:
- pages _____, as originally filed/furnished
- pages* _____, as amended (together with any statement) under Article 19
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ the drawings:
- pages _____, as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

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International application No.

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 12-22

because:

- ☒ the said international application, or the said claims Nos. 12-22
relate to the following subject matter which does not require an international preliminary examination (*specify*):

The subject matters of claims 12-22 relate to methods for treatment of the human body by therapy, which do not require an international preliminary examination by the International Preliminary Examining Authority in accordance with PCT Article 34(4)(a)(i) and PCT Rule 67.1(iv).

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. 12-22

- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the
Administrative Instructions in that:

- | | |
|----------------------------|------------------------------------------------------------|
| the written form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with
the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☐ see Supplemental Box for further details.

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	27-32	YES
	Claims	1-11, 23-26	NO
Inventive step (IS)	Claims		YES
	Claims	1-11, 23-32	NO
Industrial applicability (IA)	Claims	1-11, 23-32	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Documents:

Document 1: WO, 01-14557, A1 (Dana-Farber Cancer Institute, Inc.), 1 March, 2001 (01.03.01)

Document 2: WO, 02-00730, A2 (Genetics Institute, Inc.), 3 January, 2002 (03.01.02)

Document 3: WO, 02-00692, A2 (Genetics Institute, Inc.), 3 January, 2002 (03.01.02)

Document 4: EP, 670369, A2 (Ono Pharmaceutical Co., Ltd.), 6 September, 1995 (06.09.95)

Document 5: Blockade of PD-1 Ligands on Dendritic Cells Enhances T Cell Activation and Cytokine Production (Julia A. Brown, et al.), FASEB Journal, March 2002, Vol. 16, No. 4, pages A710 and 517.4

Explanation:

The subject matters of claims 1-11 and 23-26 relate to the use of a substance to inhibit immunosuppressive signals of PD-1, PD-L1 or PD-L2 for the purpose of manufacturing immunopotentiator compositions and anticancer compositions. Document 1 (Abstract, the claims, page 82, line 8 to page 86, line 10), document 2 (Abstract, the claims, page 104, line 9 to page 108, line 13), document 3 (Abstract, the claims, page 104, line 9 to page 108, line 13), document 4 (Abstract, the claims, page 5, line 52 to page 6, line 6), and document 5 describe the use of a substance of inhibiting immunosuppressive signals of PD-1, PD-L1 or PD-L2. Accordingly, the subject matters of claims 1-11 and 23-26 do not appear to be novel.

The subject matters of claims 27-33 relate to (1) cancer cell lines for screening that are so transformed as to have PD-L1 or PD-L2 expressed, (2) methods of screening immunopotentiators by means of such cells, (3) mammals created by transplanting such cell lines, and (4) methods of selecting anticancer substances by means of the said mammals; but documents 1-5 do not describe them. In the field of drug development, however, a person skilled in the art could have easily conceived of a method of screening inhibitors by using the substances to be inhibited, or a system of cell lines or animals to have such inhibitors expressed, and so in view of the descriptions of documents 1-5 meaning that substances inhibiting immunosuppressive signals of PD-1, PD-L1 or PD-L2 have an immunopotentiating effect and an anticancer effect, (1) cancer cell lines for screening that are so transformed as to have PD-L1 or PD-L2 expressed, (2) methods of screening immunopotentiators by means of such cells, (3) mammals created by transplanting such cell lines, and (4) methods of selecting anticancer substances by means of the said mammals, would be obvious to a person skilled in the art.

Accordingly, the subject matters of claims 27-33 do not appear to involve an inventive step.

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Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 03/042402 A2 [E, X]	22.05.2003	12.12.2002	13.12.2001
WO 03/011911 A1 [E, X]	13.02.2003	30.07.2002	31.07.2001
WO 02/078731 A1 [E, X]	10.10.2002	02.04.2002	02.04.2001

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)